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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,206	01/02/2002	Jasper Rine	UOCB118456	1317
26389	7590	01/16/2004		
CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC 1420 FIFTH AVENUE SUITE 2800 SEATTLE, WA 98101-2347				
			EXAMINER BRUSCA, JOHN S	
			ART UNIT 1631	PAPER NUMBER

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/038,206

Applicant(s)

RINE ET AL.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Oath/Declaration

1. The instant application contains a Rule 63 Declaration originally executed in claimed parent Application No. 08/512753 and a single unsigned power of attorney filed in claimed parent application 09/294453 designating Christensen, O'Connor, Johnson, & Kindness PLLC as agents of record. Also attached is a copy of a letter from the USPTO dated 29 February 2000 acknowledging the above power of attorney in Application No. 09/294453. The instant application has been given a correspondence address of Christensen, O'Connor, Johnson, & Kindness (customer No. 26389) as directed on the transmittal papers of the instant application filed. Prosecution will proceed under 37 CFR 1.34(a) with the above named law firm. The applicants are requested to file a signed power of attorney in the instant application in view of 37 CFR 1.63(d)(4) cited below:

37 CFR 1.63. Oath or declaration.

(d)

(4) Where the power of attorney (or authorization of agent) or correspondence address was changed during the prosecution of the prior application, the change in power of attorney (or authorization of agent) or correspondence address must be identified in the continuation or divisional application. Otherwise, the Office may not recognize in the continuation or divisional application the change of power of attorney (or authorization of agent) or correspondence address during the prosecution of the prior application.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claim 69 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 69 is drawn to data in computer readable memory which is not patentable subject matter (see MPEP 2106).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 38-53, 55-66, 68-83, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gress et al. in view of Granelli-Piperno et al. in view of Fodor et al.

The claims are drawn to a method of assay of the response of a living thing to a stimulus by use of an array of probes comprising a predetermined sequence of nucleotides to individual gene transcripts by comparing databases comprising results of hybridizations of labeled

polynucleotides derived from cells either treated with different stimuli or unstimulated control cells, the database produced by the method, and methods of generating the database produced by the method. The responses are measured by converting an output signal to an electrical signal and then converting the electrical signal to a value in a database. In some embodiments at least 50% of the gene transcripts of the cell are assayed, the cells are human cells, the probes consist of 24-240 nucleotides, and the database is computer implemented. In some embodiments the probes are in an X and Y coordinate grid. In some embodiments the method is repeated for different stimuli.

Gress et al. shows throughout, and especially on page 609 and figure 3 a general method of assaying patterns of transcription by use of labeled cDNA from mouse, and human cells by use of a cDNA X-Y coordinate grid array of probes. The array provides an optical signal of expression in an assayed human cell of individual genes in the cell. Gress et al. shows importing the resulting data via an electrical signal of a Phosphorimager to a computer implemented relational database on page 616. Gress et al. shows in the abstract that their high density array allows for the efficient assay of thousands of clones simultaneously. Gress et al. shows on page 612 that polyA control probes hybridize non-specifically to many array cDNA probes and that other cDNA probes in the array contained repetitive sequences that also caused non-specific hybridization. Gress et al. shows on page 616 that one strategy to avoid background non-specific hybridization is to use probes that lack polyA tails by use of modified primers. Gress et al. does not show subsection of assayed cells to different stimuli, or comparison of the transcriptional profile of cells that have received different stimuli, or assay of discrete portions of the complete number of genes of the cell, or use of probes with a predetermined sequence of nucleotides.

Granelli-Piperno et al. shows in figures 1-9 the effect of a variety of compounds on expression of genes of human cells. The tested compounds include cytokines, mitogens, cyclosporin A, and cycloheximide. The response is determined by the intensity of a film image on an autoradiograph. Granelli-Piperno et al. show that assay of expression of genes after treatment of cells with drugs allows a determination of the effect of the drug on individual gene expression and further serves to gain insights on the mechanism of action of the drug. Granelli-Piperno et al. shows a database in Table 1 of the results of their assays, which include inductions of cytokine mRNA by lectins and repression of cytokine mRNA by cyclosporin A.

Fodor et al. shows throughout a method of making an array of polynucleotide probes of predetermined sequence by independent in situ stepwise synthesis of each oligonucleotide probe on the array. Fodor et al. shows in columns 32, lines 12-24 that their arrays may be used to map the location of a molecule on a chromosomal map. Fodor et al. shows in column 35 that their procedure may be used to assay the developmental stage cells from which the assayed sample is derived. In column 78-79, Fodor et al. shows that their method may be used to assay developmental stages of cells by assay of their mRNA content.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Gress et al. by assaying cells that have received treatments with different drugs according to the method of Granelli-Piperno et al. because Granelli-Piperno et al. shows that such an analysis serves to gain insights on the mechanism of action of the drug. It would have been further obvious to assay additional numbers of genes as desired to determine the effect of a drug on additional genes. Regarding the size of the probes, it would have been obvious to use portions of a cDNA probe of Gress et al. because Gress et al.

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shows that many array probes suffer from non-specific hybridization due to repetitive sequences of polyA tracts and that the problem may be solved by use of shorter probes. It would have been further obvious to use an array of probes with a predetermined sequence as disclosed by Fodor et al. because Fodor et al. shows that such an array has the advantage of allowing the sequences detected in the sample to be mapped to a particular location of the genome of the organism sampled. Regarding the limitations of claims 71 and 72, it would be further obvious to one of skill in the art to perform simple mathematical comparisons of the levels in stimulated and control cells such as subtraction or division by the basal level to reveal the extent of change in the level of the assayed mRNA.

6. Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gress et al. in view of Granelli-Piperno et al. in view of Fodor et al. as applied to claims 38-53, 55-66, 68-83, and 85 above, and further in view of Watson et al.

The claims are drawn to assays utilizing fungal cells.

Watson et al. shows on pages 573-575 that yeast cells contain genes that are regulated by stimuli such as metabolites.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Gress et al. in view of Granelli-Piperno et al. in view of Fodor et al. as applied to claims 38-53, 55-66, 68-83, and 85 above by using yeast gene probes and cells because Watson et al. shows that yeast cells have genes that are regulated by stimuli.

Double Patenting

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7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 38, 43-50, 56, 59, 62-65, 70, 74, 77, 79, and 80-82 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 6, 13, 15, 16, 19, 26, and 28 of U.S. Patent No. 5,777,888 in view of Fodor et al.

The claims are drawn to a method of assay of the response of a living thing to a stimulus by use of an array of probes comprising a predetermined sequence of nucleotides to individual gene transcripts by comparing databases comprising results of hybridizations of labeled polynucleotides derived from cells either treated with different stimuli or unstimulated control cells, and methods of generating the database produced by the method. The responses are

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measured by converting an output signal to an electrical signal and then converting the electrical signal to a value in a database. In some embodiments at least 50% of the gene transcripts of the cell are assayed, the probes are in an X and Y coordinate grid, and the method is repeated for different stimuli.

U.S. Patent No. 5,777,888 claims in claims 1, 13, 16, and 26 a method of analyzing a transcriptional profile and of making a database of a transcriptional profile by use of an array of probes to assay samples of a cell that has been stimulated. U.S. Patent No. 5,777,888 claims in claims 6, 15, 19, and 28 methods in which the majority of transcripts are assayed. U. S. Patent No. 5,777,888 does not claim a method that uses an array of probes of a predetermined sequence of nucleotides.

Fodor et al. shows throughout a method of making an array of polynucleotide probes of predetermined sequence by independent in situ stepwise synthesis of each oligonucleotide probe on the array. Fodor et al. shows in columns 32, lines 12-24 that their arrays may be used to map the location of a molecule on a chromosomal map. Fodor et al. shows in column 35 that their procedure may be used to assay the developmental stage cells from which the assayed sample is derived. In column 78-79, Fodor et al. shows that their method may be used to assay developmental stages of cells by assay of their mRNA content.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of U.S. Patent No. 5,777,888 claims 1, 6, 13, 15, 16, 19, 26, and 28 to use an array of probes with a predetermined sequence as disclosed by Fodor et al. because Fodor et al. shows that such an array has the advantage of allowing the sequences

detected in the sample to be mapped to a particular location of the genome of the organism sampled.

Response to Arguments

9. Applicant's arguments filed 04 November 2002 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The applicants state that Gress et al. shows only hybridization fingerprinting rather than arrays with fragments of known or identified genes, but the claims only require that the probes in the array hybridize with genes of the assayed cell, as shown by Gress et al. The applicants state that Gress et al. shows mapping rather than gene expression assays, however Gress et al. shows comparisons of gene expression levels for different assayed genes in figures 2 and 3. The applicants state that Granelli-Piperno et al. shows use of northern blots rather than arrays but Granelli-Piperno was cited for showing transcriptional analysis of stimulated versus control cells. The applicants state that the probes of Fodor et al. are not specific, but do not provide evidence to support the assertion. The applicants question whether the applied references show a database, but Granelli-Piperno et al. shows a database in Table 1, and Gress et al. discuss a relational database of their data on page 610-611. The applicants point to the limitations of claim 38 requiring comparison of data, but such data comparisons are obvious to one of ordinary skill in the art to determine the effect of the stimulus, as is repetition of steps of the method.

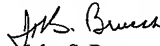
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Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00. On approximately 12 January 2004 Art Unit 1631 will move to the new USPTO Alexandria, VA facility. At that time the phone number of the examiner will change to (571) 272-0714. Phone calls to the previous phone number will be referred to the new phone number for 60 days after the move date.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4028. The fax phone number for the organization where this application or proceeding is assigned is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.


John S. Brusca
Primary Examiner
Art Unit 1631

jsb